## THE REMARKS

### The Amendments

The specification is amended to correct the use of trademarks.

Claim 35 is amended to recite that wherein the first and second primary antibodies antibody are obtained from different animals selected from the group consisting of mice, rats, rabbits, sheep, and goats. Support for the amendment can be found at page 16, lines 22-24; page 22, lines 12-14; page 29, lines 1-2 and 9-10.

The amendment in Claim 36 is supported by page 20, lines 13-14, and page 21, lines 10-11.

The amendments in Claims 37 and 47 are supported by page 10, line 21, through page 11, line 4; and page 26, lines 14-17.

New Claim 48 is supported by page 15, line 27 through page 16, line 2; and page 22, lines 12-18.

New Claim 49 is supported by page 22, lines 12-13; page 30, lines 11 and 18.

No new matter is introduced in any of the amendments. The Examiner is requested to enter the amendments.

### The Response

**Objection to the Specification**

7. The specification is objected to because the use of improperly demarcated trademarks has been noted in this application.

Applicants have amended the specification to correct the defects.

**Claims Objections**

8. Claims 37, 38, and 40 are objected to as allegedly being drawn in the alternative to the subject matter of non-elected species of invention.

Claim 40 is cancelled. Claims 37 and 38 are amended to be proper dependent claims of the elected species.

9. Claim 41 is objected to under 37 CFR 1.75(c), as allegedly being of improper dependent form for failing to further limit the subject matter or a previous claim.

Claim 41 is cancelled.

**35 U.S.C. §112, Second Paragraph, Rejections**

11. Claims 42-45 are rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 42 and 43 amended to depend on Claim 39.

Claims 44 and 45 are cancelled.

**35 U.S.C. §112, First Paragraph Rejections**

13. Claims 35-41 are rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement. The rejection is overcome in view of the claim amendments.

The Examiner states that "probe" might be any molecule (e.g., a peptide, a small organic molecule or any a ligand of any other material or structure), which might be used to detect $p16^{INK4a}$ and/or Ki-67. Applicants have amended the claims to change "probes" to "antibodies."

The Examiner further states that although $p16^{INK4a}$ and Ki-67 may be fully characterized antigens, the claims are not limited to an antibody that binds $p16^{INK4a}$ or Ki-67, but includes any antibody that binds to any one of a genus of "INK4a polypeptides" and any antibody that bind to any one of a genus of "cell proliferation polypeptide markers." Applicants have amended the claims to recite $p16^{INK4a}$ polypeptide and Ki67 polypeptide.

Therefore, the 35 U.S.C. §112, first paragraph rejection for lack of written description should be withdrawn.

14. Claims 35-41 are rejected under 35 U.S.C. §112, first paragraph, because the specification, while being enabling for making and using a kit comprising an antibody that specifically binds to $p16^{INK4a}$ and an antibody that binds to the Ki-67/Ki-S5 antigen, does not allegedly provide enablement for making and/or using the claimed kits, which comprise one or

more "probes" for the detection of the expression of at least one "INK4a polypeptide" and one or more "probes" for the detection of at least one "cell proliferation polypeptide marker."

Applicants have amended the claims to recite $p16^{INK4a}$ polypeptide, Ki67 polypeptide, and antibodies against them.

Therefore, the 35 U.S.C. §112, first paragraph rejection for non-enablement should be withdrawn.

**35 U.S.C. §103(a) Rejection**

16. Claims 35-41 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Martin et al. (*Am. J. Pathol.* 2000 May; 156 (5): 1573-1579). The rejection is overcome in view of the claim amendment.

Martin et al. (page 1574, right column) disclose first incubating tissue sections with mouse anti-Ki-67 antibody, then detecting Ki-67 by peroxidase-labelled goat anti-mouse Ig. After the above steps were completed, the tissue sections were rinsed and then incubated with mouse anti-p16/INK4a, and detected by phosphatase-labeled goat anti-anti-mouse Ig. Martin et al's method requires multiple steps and handling.

Claim 35 is directed to a kit comprising a first primary antibody against $p16^{INK4a}$ polypeptide, and (b) a second primary antibody against Ki67 polypeptide, wherein the first and second primary antibodies antibody are obtained from different animals selected from the group consisting of mice, rats, rabbits, sheep, and goats. Martin et al. do not teach or suggest that the two primary antibodies are obtained from different animals.

The advantages of Claim 35 are that a sample can be simultaneously incubated with the two primary antibodies. Because the two primary antibodies are obtained from different animals, the sample can then be simultaneously incubated with two different secondary antibodies and detected for $p16^{INK4}$ and Ki-67.

Claim 39 is directed to a kit comprising (a) a first antibody against $p16^{INK4a}$ polypeptide, and (b) a second antibody against Ki67 polypeptide, wherein said first and second antibody are labelled with distinguishable labels. Martin et al. do not teach or suggest that the anti-$p16^{INK4a}$ antibody and the anti-Ki67 antibody are labeled with distinguishable labels.

Therefore, the 103(a) rejection of Claims 35, 39 and their dependent claims should be withdrawn.

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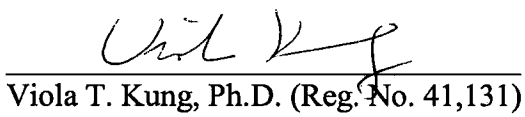
Respectfully submitted,



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